

Answer 1:

Bibliographic Information

Beneficial Effects of Costimulatory Blockade with Anti-Inducible Costimulator Antibody in Conjunction with CTLA4Ig on Prevention of Islet Xenograft Rejection from Rat to Mouse. Nabeyama, Kentaroh; Yasunami, Yohichi; Toyofuku, Atsushi; Nakano, Masahiko; Satoh, Masayuki; Matsuoka, Nobuhide; Ono, Junko; Kamada, Masafumi; Uede, Toshimitsu; Todo, Satoru; Ikeda, Seiyo. Department of Surgery I, Fukuoka University School of Medicine, Fukuoka, Japan. Transplantation (2004), 78(11), 1590-1596. Publisher: Lippincott Williams & Wilkins, CODEN: TRPLAU ISSN: 0041-1337. Journal written in English. CAN 142:296409 AN 2004:1059869 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

BACKGROUND: Costimulatory signals have been reported to play an important role in islet-xenograft rejection, although the precise mechanisms remain unknown. The aim of the present study was to det. a role of a novel costimulatory mol., inducible costimulator (ICOS), in rat islet-xenograft rejection in conjunction with CTLA4Ig with respect to cellular as well as humoral immune responses. **METHODS:** Isolated rat islets were transplanted into the liver of streptozotocin (180 mg/kg) induced diabetic mice. Cellular immune responses to islet xenografts, and productions of anti-rat antibody in mice were examd. by flow cytometry (FACS) after transplantation. **RESULTS:** Intrahepatic rat islet xenografts were rejected in mice within 8 days after transplantation. FACS anal. revealed an expansion of CD8+ cells in the liver as well as a prodn. of anti-rat antibody in recipient mice in assocn. with rejection. The treatment with anti-ICOS antibody in conjunction with CTLA4Ig produced a marked prolongation of islet-xenograft survival with neither expansion of CD8+ T cells nor prodn. of anti-rat antibody, whereas, in contrast, those treated with anti-ICOS antibody or CTLA4Ig alone did not have prolonged survival, and CD8 T cells were expanded. **CONCLUSION:** These findings demonstrate that cellular rather than humoral immune responses are considered responsible for islet-xenograft rejection from rat to mouse and that the blockade of costimulatory signals with anti-ICOS antibody in conjunction with CTLA4Ig has a favorable effect on prevention of islet xenograft rejection.

Answer 2:

Bibliographic Information

Graft survival and MLC response in LEW-ACI small bowel transplants treated with a novel MHC peptide, BC-1nI. Tice, D. G.; Bruch, D.; Squiers, E. C. Transplant Program, Department of Surgery, SUNY HSC, Syracuse, NY, USA. Transplantation Proceedings (1998), 30(6), 2590-2591. Publisher: Elsevier Science Inc., CODEN: TRPPA8 ISSN: 0041-1345. Journal written in English. CAN 130:60762 AN 1998:675903 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Small synthetic peptides corresponding to polymorphic regions of the human HLA-B7-01 mol. have non-MHC-restricted immunomodulatory effects both in vitro and in vitro. In vitro, ALLOTRAP inhibits differentiation of CTL and inhibits CTL and natural killer (NK) lysis. In vivo, ALLOTRAP prolongs LEW.1W > LEW.1A heart allograft survival, prolongs LEW > ACI heart allograft survival when used in combination with cyclosporine, and prolongs the survival of C57BL/6 > CBA murine skin allografts. We have obsd. that ALLOTRAP administered together with anti-lymphocyte serum significantly prolonged porcine islet xenograft survival in streptozocin-treated or NOD mice (unpublished observations). We therefore have asked whether there would be any immunomodulatory effects of BC-1nI, a synthetic peptide of the ALLOTRAP family, on survival of LEW small bowel allografts in ACI rats. Although BC-1nI did not induce long-term allograft survival or tolerance in highly immunogenic small bowel transplant model, use of small mol. wt. HLA-derived peptides as immunosuppressive agents remains as interesting possibility in the less immunol. stringent allograft models.

Answer 3:

Bibliographic Information

Induction of tolerance to islet xenografts in a concordant rat-to-mouse model. Goss J A; Nakafusa Y; Finke E H; Flye M W; Lacy P E Department of Surgery, Washington University School of Medicine, St. Louis, MO 63110 Diabetes (1994), 43(1), 16-23. Journal code: 0372763. ISSN:0012-1797. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 8262312 AN 94085699 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Induction of tolerance to concordant rat islet xenografts (150 Wistar-Furth [WF] islets) in streptozocin-induced (STZ) diabetic mice (C57BL/6) was determined at three different sites for islet implantation (thymus, kidney capsule, and liver). Islets transplanted into the thymus or kidney capsule were either fresh or cultured at 24 degrees C for 7 days, and the mice received a single injection of either anti-mouse lymphocyte serum (MALS) alone or anti-rat lymphocyte serum (RALS) and MALS. Islets transplanted into the liver via the portal vein were cultured at 24 degrees C for 7 days, and the mice received a single injection of MALS and RALS. To document the induction of tolerance, recipients with islet xenografts surviving > 100 days were made diabetic again by STZ (thymus and liver) or nephrectomy (kidney capsule) and received a second transplant of 150 fresh WF islets in the kidney capsule. Kidney capsule placement of fresh or cultured islets with MALS alone or MALS and RALS did not induce tolerance in a significant number of recipients. The intrathymic transplantation of fresh or cultured islets with MALS alone resulted in prolonged WF islet xenograft survival (mean survival time of 39.7 +/- 7.9 days) but did not result in tolerance, whereas the administration of MALS and RALS with the intrathymic placement of fresh or cultured islets induced tolerance in approximately 50% of the mice. Intrahepatic transplantation of cultured islets with MALS and RALS resulted in tolerance to donor islets in 90% of the recipients. Donor specificity was evaluated by a third major histocompatibility complex-disparate fresh Lewis islet xenograft.(ABSTRACT TRUNCATED AT 250 WORDS)